Second internship program of APAC Natural Product Drug Discovery Consortium(ANPDC)

Supawan Jamnongsong

SiCORE for Systems Pharmacology

Workflow of program

Phase 1:
- Tech-transfer for HTS
- Tech-transfer for cortical Differentiation method for capacity building

Phase 2:
-Phenotypic screening in Thailand

Takeda pharmaceutical company
- Training period: Feb-April 2020

iPark

Second internship program of APAC Natural Product Drug Discovery Consortium(ANPDC)

Tech-transfer by
by Hidehisa Iwata's reseach group

Hidehisa Iwata

- **Macropinocytosis assay for natural product screening**

- **Cell reprogramming and differentiation method (iPSC-- > NPC-- > neuron)**

Masayo Saito

Hiroaki Nagai

Second internship program of APAC Natural Product Drug Discovery Consortium(ANPDC)

SiSP

Tech-transfer items

Takeda

Hiroaki Nagai

Masayo Saito

- **Macropinocytosis assay for natural product screening**

Phase1: Capability building of Thailand researcher for macro-pinocytosis activator/inhibitor screening
- establish pipeline for detection both activator and inhibitor features.
- identify best activator control using 26 candidate compounds

Phase2:Evaluation of natural products (around 3000 cpds) in Thailand (collaborate with ECDD)
- writing proposal for budget request
- setting platform for compound screening at ECDD
- perform compound libraries
- make decision for further collaboration

- **Cell reprogramming and differentiation method (iPSC-- > NPC-- > neuron)**

Phase1: Capability building of Thailand researcher for forebrain cortical neuron differentiation method (using Shi-method)
- iPS/NPC : maintain and collect frozen stock
- Neurons: maintain and characterization

Phase2:
- use neuron for study in neurodgenerative diseases (optional)
- collaborate with other teams in NPDD groups

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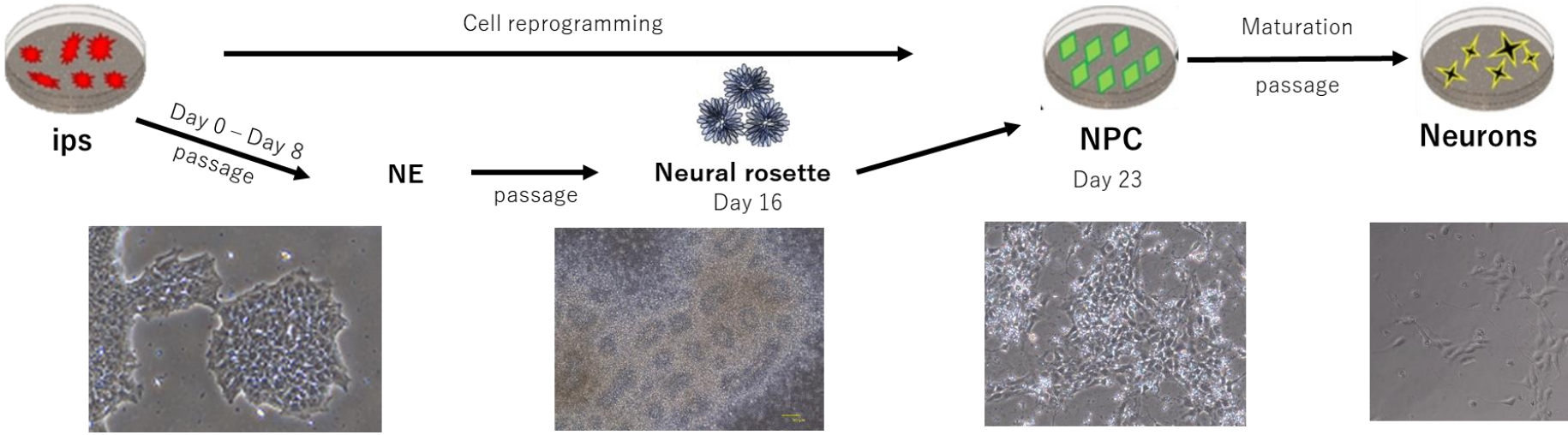
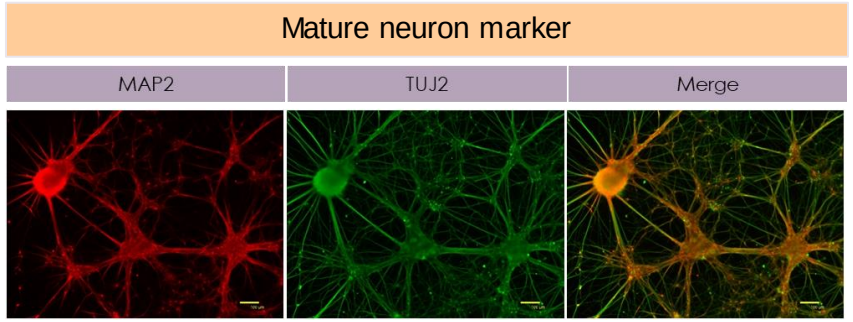
Masayo Saito

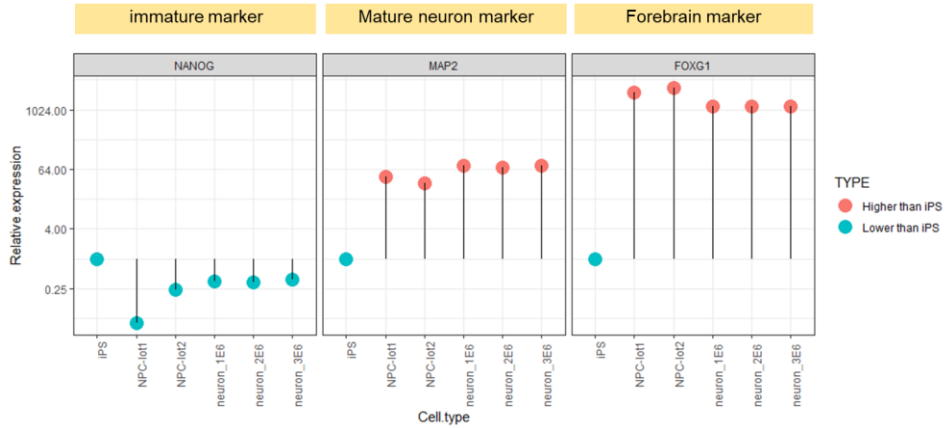

Supawan Jamnongsong

- **Cell reprogramming and differentiation method (iPSC-- > NPC-- > neuron)**



Characterization of human iPS-derived cortical neurons





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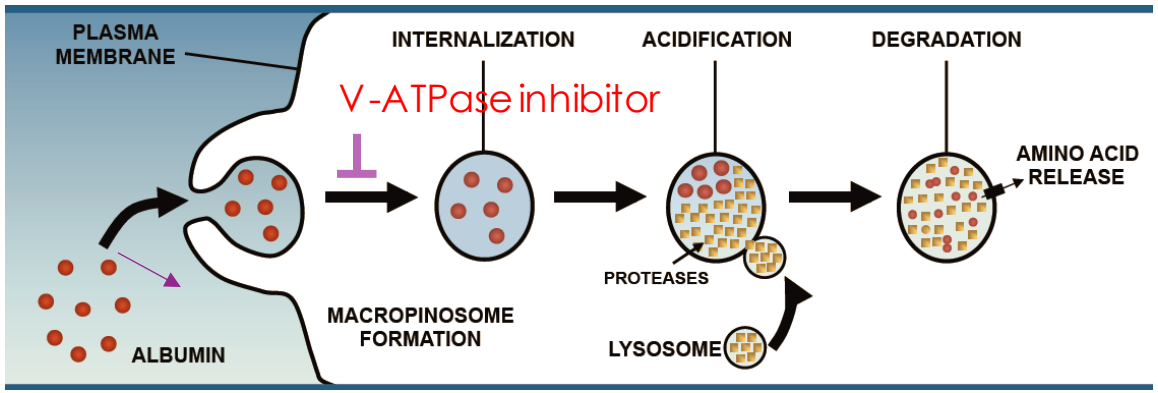
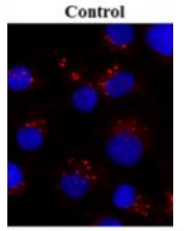
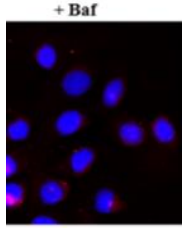


TMR-BSA



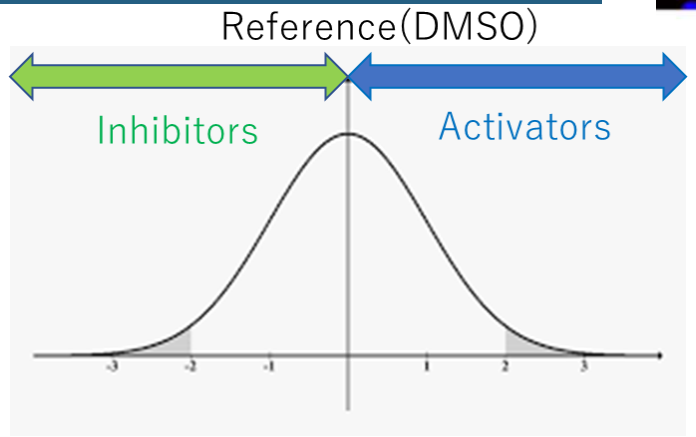


Hiroaki Nagai

Supawan Jamnongsong

Macropinocytosis inhibitors: finding therapeutic option for cancers

Using known inhibitor which identified by Takeda pharmaceutical company



Macropinocitosis activity

Macropincotosis activators: seeking a new approaches for drug delivery system for neuroscience area

Identify best activator control using 26 candidate compounds

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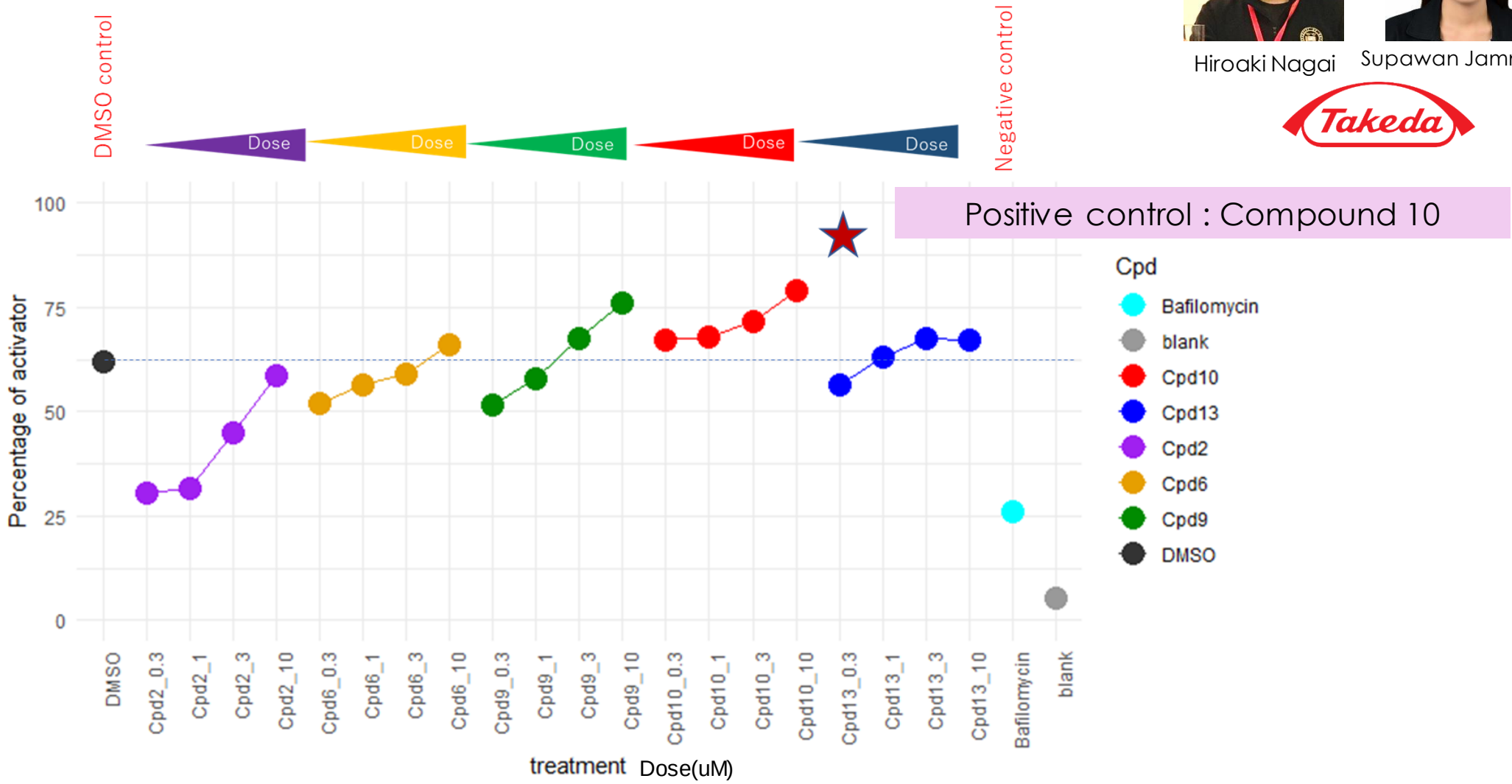
Hiroaki Nagai

Supawan Jamnongsong

Takeda

- **Macropinocytosis assay for natural product screening**



Phenotypic screening of natural products for potential use in Neurology, Oncology area and DDS via macropinocytosis

Collaborative workflow: Phenotypic screening in Thailand

TCELS Thailand Center of Excellence for Life Sciences

BIOTEC a member of NSTDA

Chulalongkorn University

Proposal submission

↓

TCELS-Takeda / TCELS-Siriraj Research agreement

↓

Takeda pharmaceutical company

Tech-transfer

↓

Positive compound transfer to Thailand (MTA)

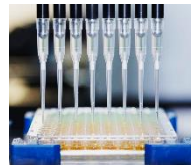
→

SiSP Siriraj Initiative in Systems Pharmacology

Natural product library

↓ Collect by ECDD

Natural product library screening facility



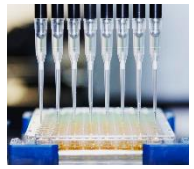
↓ Screening at

ECDD Excellent Center for Drug Discovery

Phenotypic screening of natural products for potential use in Neurology, Oncology area and DDS via macropinocytosis

Collaborative workflow: Phenotypic screening in Thailand

Thai Natural products



Collect natural product and prepare library

Optimize and plate reformatting

Macropinocytosis screening with natural product

Imaging by high content imager/ image analysis and data processing

BIOTEC a member of NSTDA

Chulalongkorn University

ECDD Excellent Center for Drug Discovery

Excellent Center for Drug Discovery

SiSP

Siriraj Initiative in Systems Pharmacology

ECDD Excellent Center for Drug Discovery

Excellent Center for Drug Discovery

SiSP

Siriraj Initiative in Systems Pharmacology

Dr. Suparerk Borwornpinyo (Director ECDD)

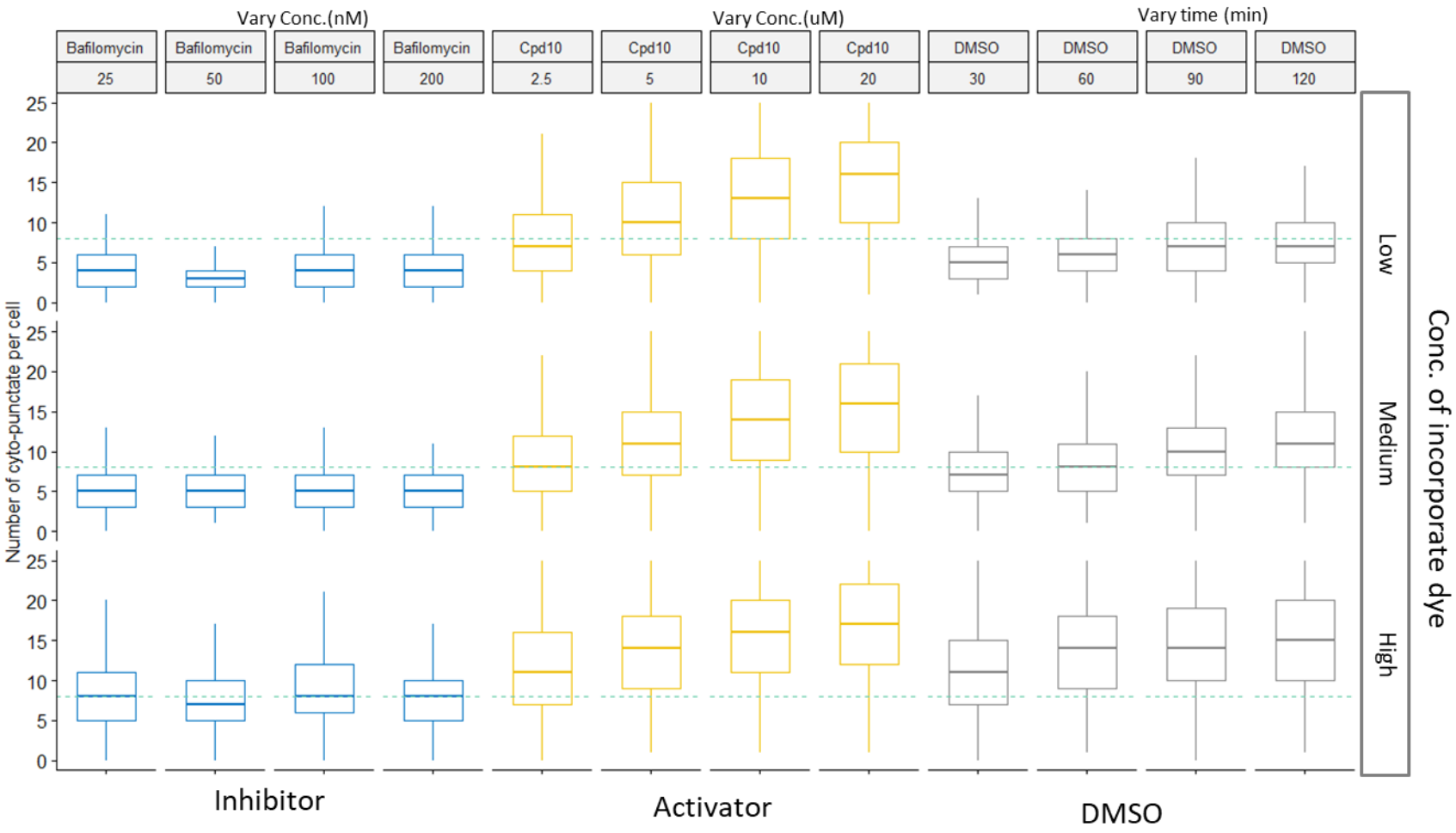
Dr. somponnat sampattavanich (Director SiSP)

Phongthon Kanjanasirirat (first internship)

Supawan Jamnongsong (Second internship)

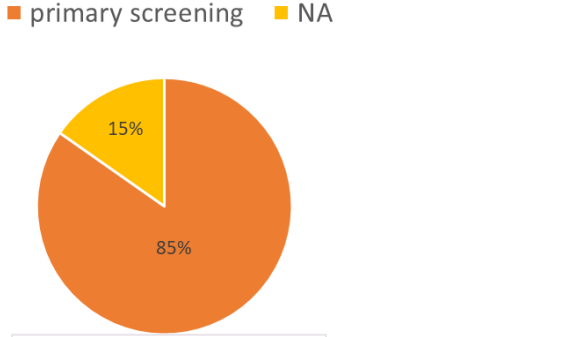
Phenotypic screening of natural products for potential use in Neurology, Oncology area and DDS via macropinocytosis

Phenotypic screening in Thailand: optimization

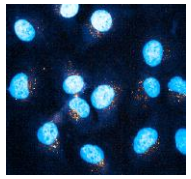


Phenotypic screening of natural products for potential use in Neurology, Oncology area and DDS via macropinocytosis

Phenotypic screening in Thailand: primary screening



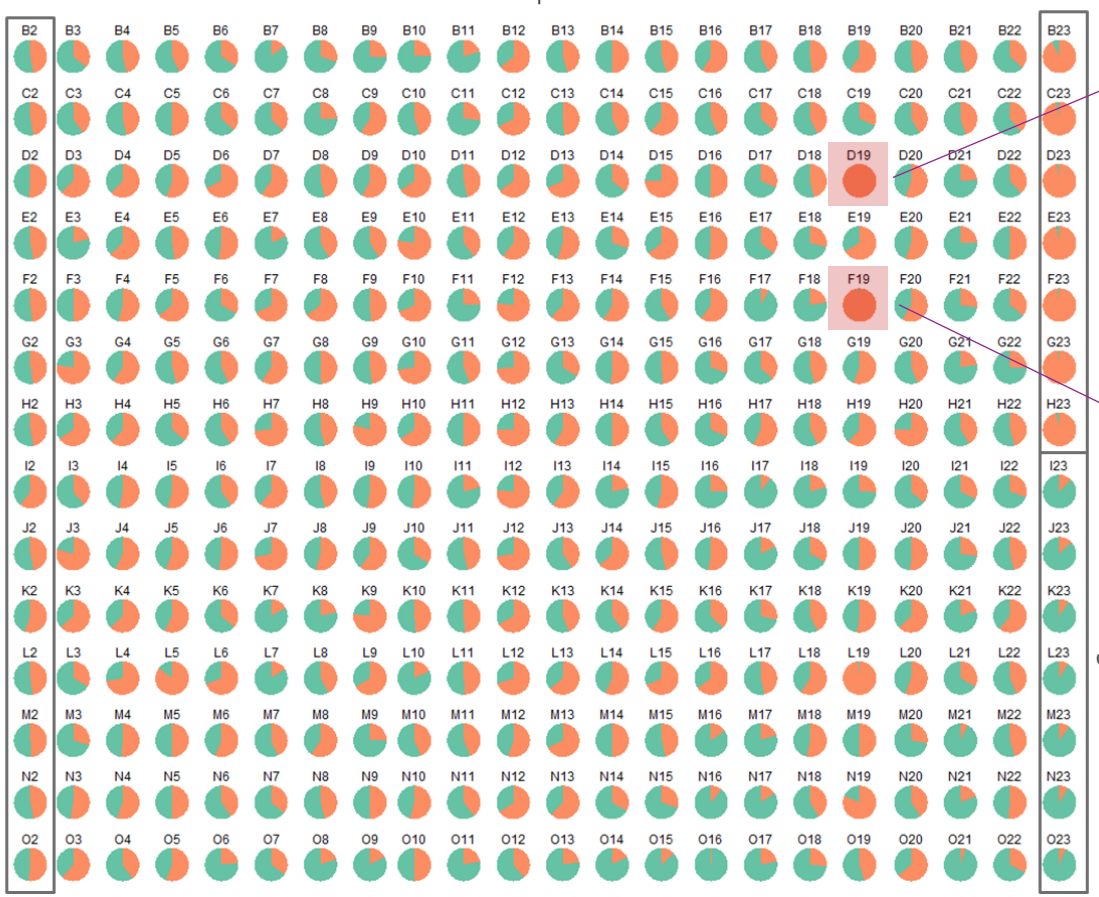
- total 2588 compounds
- screened 85% (2192 Compounds)



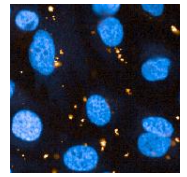
DMSO control

Candidate 8 hit compounds

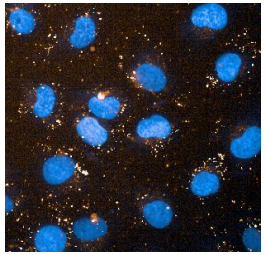
future confirm with secondary screening



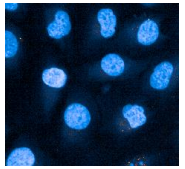
Positive control



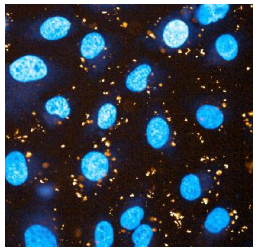
Candidate activator



Negative control



Candidate activator



Phenotypic screening of natural products for potential use in Neurology, Oncology area and DDS via macropinocytosis

Phenotypic screening in Thailand: Hit identification

progression

85 % of primary screening

Primary screening of ECDD libraries in cell model for macropinocytosis activity (2588 compounds)

>70% inhibition or activation, reproducibility, no interference with incorporate dye

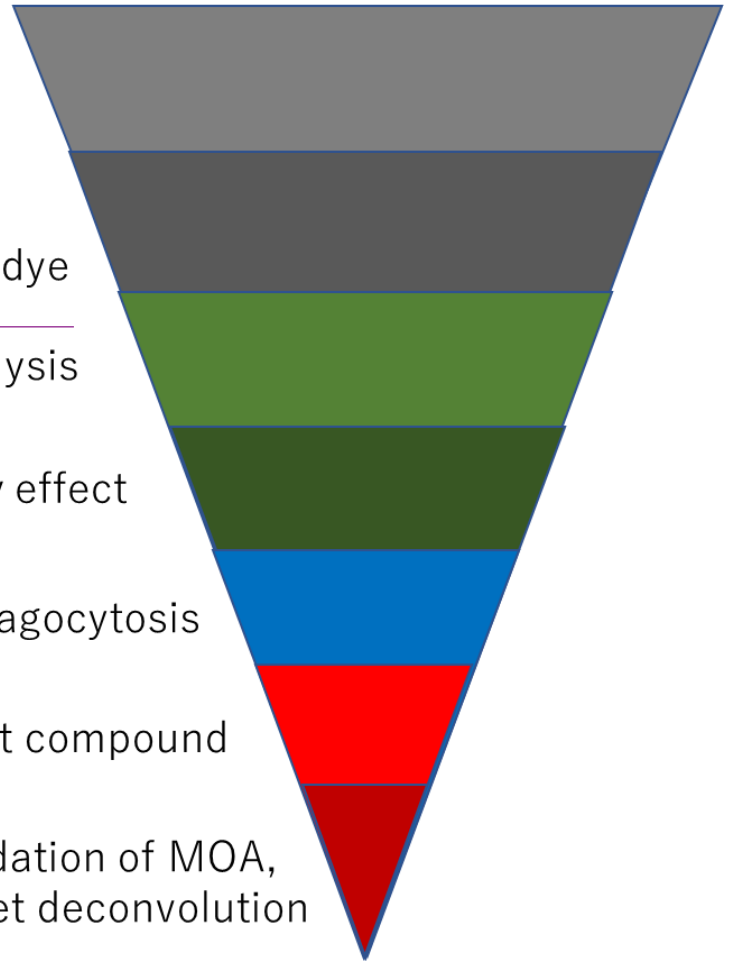
Secondary screening with dose response analysis

No cytotoxicity effect

No inhibitory or activating effects on receptor-mediated endocytosis or phagocytosis

Identify hit compound

Characterization assay for elucidation of MOA, Structure determination and target deconvolution



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